daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid. --

REMARKS

Claims 1-3, and 69-86 are pending. Applicants amend claims 1-3 and 70-72, 77-81, 83-86 herein. Accordingly, claims 1-3 and 69-86 are being examined. Entry of amended claims 1-3 and 69-86 is respectfully requested.

The amendment of claims 70, 77-81 and 83-86 merely corrects the dependency from a previous claim. These amendments do no involve new matter and entry of these amendments is respectfully requested.

A copy of the claim changes are attached as "Version with Markings to Show Changes in the Claims".

Oath/Declaration

In paragraph 6 at page 2 of the Office Action, the Patent Office alleges that the oath/declaration is defective. Applicants filed a corrected Declaration with the Patent Office on June 11, 2001. Applicants provide herein a copy of the corrected Declaration and the accompanying return postcard which is date-stamped June 15, 2001 by the Patent Office (Exhibit 1; 11 pages).

Rejections Withdrawn

Applicants are pleased that in paragraphs 7 and 8, the Patent Office has withdrawn the rejections of: (1) claims 4-5 under 35 USC §112, second paragraph; and (2) claims 1-5 and 9-11 under 35 USC §102(e) in view of Au Young (US Patent No. 5,856,136).

A. RESPONSE TO ARGUMENTS

Priority

The Patent Office has accorded priority to the claims as set forth in paragraph 9. Applicants disagree with the priority the Patent Office has accorded to claims 2, 69-70, 71-72, 75, 80, 82, 83, and 85. These claims are entitled to have the benefit of earlier filing dates based on the disclosure of earlier-filed patent applications which the subject application claims priority.

Priority of Claim 2:

The Patent Office granted the priority date of December 2, 1998, for claim 2 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

Claim 2 recites monoclonal antibodies which bind the middle portion of PSCA. Support for claim 2 can be found at the following: the originally-filed specification of U.S. Serial No. 09/038,261, filed March 10, 1998, at page 37, lines 9-18 and lines 23-25.

Priority Date of Claims 69 and 70 :

The Patent Office granted the priority date of December 2, 1998, for claims 69 and 70 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

Claim 69 recites monoclonal antibodies which are chimeric antibodies. Claim 70 recites chimeric antibodies comprising a murine immunoglobulin variable region and a human immunoglobulin constant region. Support for claims 69 and 70 can be found at the following: the originally-filed specification of U.S. Serial No. 09/038,261, filed March 10, 1998, at the following pages: page 13, lines 29-31.

OK

Priority Date of Claims 71 and 72:

The Patent Office alleges that there is no disclosure of "human" antibodies in U.S. Serial No. 09/251,835. Applicants respectfully disagree. Support for human antibodies can be found in U.S. Serial No. 09/251,835 at page 23, lines 27-29 and page 24, lines 1-2. However, in the interest of expediting prosecution of the subject application, applicants amend claim 70.

Claim 71 has been amended herein and now recites anti-PSCA antibodies which are humanized antibodies. Claim 72 recites anti-PSCA humanized antibodies comprising a human immunoglobulin constant region. Support for claims 71 and 72 can be found at the following: the originally-filed specification of U.S. Serial No. 09/251,835, filed February 17, 1999, at page 23, lines 27-29; and page 24, lines 1-2.

OK

Priority Date of Claim 75:

The Patent Office granted the priority date of December 2, 1998, for claim 75 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

JV

Claim 75 recites fragments of anti-PSCA antibodies. Support for antibody fragments can be found at the following: the originally-filed specification of U.S. Serial No. 09/038,261, filed March 10, 1998 at page 13, lines 18-21.

Priority Date of Claim 80:

The Patent Office granted the priority date of December 2, 1998, for claim 80 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

OK

Claim 80 recites an immunotoxin where the therapeutic agent is a cytotoxic agent. Support for claim 80 can be found at the following: the originally-filed specification of 09/038,261, filed March 10, 1998, at page 12, lines 14-16; page 13, lines 33-36; and page 14, lines 1-6.

Priority Date of Claim 82:

The Patent Office granted the priority date of December 2, 1998, for claim 82 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

OK

Claim 82 recites an immunoconjugate having an anti-PSCA antibody and a therapeutic agent. Support for claim 82 can be found at the following: the originally-filed specification of 09/038,261, filed March 10, 1998, at page 12, lines 14-16; page 13, lines 33-36; and page 14, lines 1-6.

Priority Date of Claim 83:

The Patent Office granted the priority date of December 2, 1998, for claim 83 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

OK

Claim 83 recites immunoconjugates having a therapeutic agent which is a radioactive isotope. Support for claim 83 can be found at the following: the originally-filed specification of 09/038,261, filed March 10, 1998, at page14, lines 4-6.

Priority Date of Claim 85:

The Patent Office granted the priority date of December 2, 1998, for claim 85 based on the disclosure of U.S. Serial No. 09/203,939. Applicants respectfully disagree.

Claim 85 recites immunoconjugates having a therapeutic agent which is cytotoxic agent. OK Support for claim 85 can be found at the following: the originally-filed specification of 09/038,261, filed March 10, 1998, at page12, lines 14-16; page 13, lines 33-36; and page 14, lines 1-6.

DOUBLE PATENTING

In paragraph 10 of the Office Action, the Patent Office rejects claims 1-3 and 74 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 2 and 12-13 of U.S. Serial No. 09/251,835, now issued as U.S Patent No. 6,258,939.

This rejection is presently untimely. Applicants will gladly revisit this issue upon allowance of subject matter in the present case.

APPLICANTS' INVENTION:

The present invention provides monoclonal antibodies which recognize and bind particular portions of a Prostate Stem Cell Antigen (PSCA) protein.

Applicants provide data on the multiple uses of the antibodies of the invention including data showing inhibition of tumor growth and tumor burden in the prostate *in vivo*. Also, applicants' data show that the antibodies of the invention bind and inhibit growth of PSCA expressing cells of the prostate, bone, ovary, placenta, tonsils, bladder, kidney, testes, small intestines, colon, pancreas, stomach and skin. Some of the antibodies of the invention can kill tumor cells even in

an unconjugated state; at least one antibody is internalized upon binding to PSCA-expressing cells.

CLAIM REJECTIONS UNDER 35 USC §103

Au-Young in view of Green

In paragraph 11, the Examiner maintains the rejection of claims 71 and 72 under 35 U.S.C. §103(a) as allegedly unpatentable over Au-Young in view of Green.

Applicants respectfully disagree with the rejection for reasons of the record, and for additional reasons that follow:

The Legal Standards for Establishing Obviousness Under 35 U.S.C. §103

As stated in MPEP §2142, three (3) criteria must be met to establish a *prima facie* case of obviousness:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based upon applicants' disclosure.[1]

The teaching or suggestion to make the claimed combination, and the reasonable expectation of success, must both be found in the prior art, not in the Applicant's disclosure (In re Vaeck, 947

[1] MPEP §2142, *citing In re Vaeck,* 957 F . 2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Obviousness is a question of law based on findings of underlying facts relating to the prior art, the skill of the artisan, and objective considerations. See Graham v. John Deere Co., 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). To establish a prima facie case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant. In re Raynes, 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). Obviousness can not be established by hindsight combination to produce the claimed invention. In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). As discussed in Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985), it is the prior art itself, and not the applicant's achievement, that must establish the obviousness of the combination.

The teachings of the references, their relatedness to the field of the applicant's endeavor, and the knowledge of persons of ordinary skill in the field of the invention, are all relevant considerations. See In re Oetiker, 977 F.2d at 1447, 24 USPQ2d at 1445-46; In re Gorman, 933 F.2d at 986-87, 18 USPQ2d at 1888; In re Young, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). When the references are in the same field as that of the applicant's invention, knowledge thereof is presumed. However, the test of whether it would have been obvious to select specific teachings and combine them, as did the applicant, must still be met by identification of some suggestion, teaching, or motivation in the prior art, arising from what the prior art would have taught a person of ordinary skill in the field of the invention. In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596,1600 (Fed. Cir. 1988).

The Examiner Has Not Established A *Prima Facie* Case Of Obviousness

The Examiner has not established a *prima facie* case of obviousness because none of the three necessary criteria has been met. Further, none of the cited references, alone or in combination, teaches or suggests the PSCA protein as recited in the claims and thus cannot render antibodies

against particular portions or fragments of the PSCA protein obvious. Therefore, as discussed below, the pending claims are patentable over the cited references.

As discussed above, the claimed invention is directed to anti-PSCA antibodies that recognize and bind specific portions of a PSCA protein.

Au-Young did not disclose a function for PSCA

The teachings of Au-Young alone, or even if combined with the other cited references (which it should not be), are deficient to render obvious the claimed invention for the following reasons.

Au-Young teaches a theoretical/predicted amino acid sequence of PSCA protein that is 123 amino acids in length. Au-Young speculates that the PSCA protein might function like a Ly-6 molecule (Au-Young patent at column 2, lines 16-19; column 13, lines 41-47; column 16, lines 14-17; column 28, lines 13-21). However, there is no common function associated with the functionally and structurally disparate members of the Ly-6 family. For example, some Ly-6 molecules are cell surface molecules that are involved in signal transduction (e.g., Gumley et al, 1995, Immunol and Cell Biol, 73(4):277-96 (Exhibit 2)), or cell adhesion (Brakenhoff et al, 1995, J Cell Biol, 129(6):1677-1689 (Exhibit 3)). Others are secreted molecules that are involved with neurotoxicity or cytotoxicity (Tsetlin, 1999, Eur J Biochem, 264:281-286 (Exhibit 4)), or diseases unrelated to cancer (Fischer et al., 2001, Human Mol Genet, 10(8):875-880 (Exhibit 5)). Given the broad range of potential Ly-6 functions, it would not be credible to one of ordinary skill to extrapolate the function of PSCA based on the other members of the Ly-6 family. At most Au-Young provides an invitation for further research to ultimately determine whether it functions like Ly-6, and if so which type of function.

Au-Young further speculated that PSCA could be useful in cancer treatment, e.g., bladder cancer (Au-Young patent at column 18, lines 15-21). However, there is no guidance on which Ly-6 function would make PSCA useful in treating cancer in general and bladder cancer specifically. Moreover, since Au-Young did not express the PSCA protein and provides no data whatsoever

regarding the actual expression of PSCA, they could not and did not perform any experiments to determine whether this postulated function for PSCA was correct. Without more information or data, Au-Young's suggestion that PSCA has use in cancer treatment merely amounts to an invitation for further experimentation.

Au-Young merely disclosed overlapping cDNA clones containing sequences of PSCA (SCAH-2) identified from a bladder cancer cDNA library (e.g., BLADUT02; Au-Young patent at column 4, lines 50-65; and column 23, lines 65-67 and column 24, lines 1-44). The presence of PSCA cDNA in a bladder cancer library provides little information because the library contained all transcripts (including ubiquitous transcripts, housekeeping transcripts, and otherwise) and was not limited to transcripts implicated in bladder or in cancer (e.g., no subtraction library methods were described; see Au-Young patent at column 23, lines 65 and 67 and column 24, lines 1-28). Au-Young did not and could not show any correlation between the presence of PSCA transcripts and bladder or cancer in general, or bladder cancer in particular. Thus, Au-Young does not address the biological relevance of the presence of PSCA transcripts in a bladder cancer library. Au-Young did not know whether the PSCA (SCAH-2) transcripts were (1) specific to bladder cells, (2) specific to cancer cells, (3) specific to bladder cancer cells or (4) present in metastasized cells. Therefore, one of ordinary skill would not believe that PSCA was involved in bladder or cancer, let alone in bladder cancer, based on this low level of scientific data and thus start combining references to find the claimed subject matter obvious.

Au-Young did not disclose a credible use or function for PSCA. Since Au-Young provided no data supporting a particular Ly-6 function and since Ly-6 has many members, there would have been no reasonable expectation that PSCA would be useful for detection or treatment of bladder cancer or any other proposed utility. Without some credible use, there would be no motivation to make antibodies to PSCA, let alone to specific portions of PSCA.

With only a putative amino acid sequence of PSCA, and without knowing the function of the PSCA, there would be no suggestion, teaching or motivation to obtain **any** antibodies against PSCA. Moreover, without knowing the function or utility of the PSCA, the function and utility

of PSCA fragments was not be known or suggested. Accordingly, there would have been no motivation to make monoclonal antibodies of the invention that recognize particular portions of the PSCA protein.

There would have been no reasonable expectation to make the antibodies of the invention against fragments of the PSCA, using the cDNA sequence disclosed by Au-Young. For example, Au-Young teaches expressing full length PSCA in a bacterial expression system. However, bacterial expression systems commonly produce mammalian proteins as inclusion bodies containing improperly folded and aggregated protein and thus are not in its native form. Au-Young also teaches expressing full length PSCA in a mammalian expression system but does not teach how to cleave the GPI-linkage so as to produce soluble PSCA for use as an immunogen. Without more guidance, it would not have been routine to cleave the PSCA from the cell because GPI linkages exhibit differing sensitivities to GPI-cleavage enzymes. Thus even if there were a credible suggestion to one of ordinary skill to make anti-PSCA antibodies, which there was not, there would not be a reasonable expectation of success given the Au-Young disclosure.

Since Au-Young did not teach or suggest a credible use for the PSCA protein, Au-Young did not, even if it was combinable with other references, make obvious antibodies against PSCA.

The prophetic statements by Au-Young regarding generation of antibodies against full length PSCA by using any of (1) the full length PSCA (2) the C-terminal portion, (3) the hydrophilic portions of full length PSCA , or (4) 5-10 amino acid portions or fragments thereof, do not disclose or suggest the presently claimed antibodies.

As discussed above, the full length PSCA protein or portions thereof described by Au-Young do not render obvious the claimed antibodies because it cannot be obvious to make antibodies to a protein when one does not know the form in which it is expressed. Thus, Au-Young did not teach or suggest the portions of PSCA such as (a) amino acids +22 through +50; (b) amino acids +46 through +99; or (c) amino acids +85 through +99 as described in SEQ ID NO:2.

Moreover, even if Au-Young were to provide anything to one of ordinary skill more than an invitation for further research, which it does not, it is noted that Au-Young's hydrophobicity and hydrophilicity data of PSCA is not suggestive of the portions of the PSCA molecule which are recognized and bound by the antibodies of the invention.

Green Does Not Cure The Deficiency Of Au-Young

For Green to render the present invention obvious, it must cure the deficiencies of Au-Young.

Green merely teaches antigen-specific, human, monoclonal antibodies. In particular, Green teaches human monoclonal antibodies directed to tetanus toxin (page 18, first paragraph under the section entitled "Ag-specific fully human mAbs from mice").

Green does not teach or suggest the expression or function of PSCA or the portions of PSCA recognized by the antibodies of the invention and thus the combination does not render the present invention obvious.

Accordingly, there is no suggestion to combine the cited references in order to arrive at the claimed invention. Therefore, the rejection of claims 71-72 under 35 U.S.C. §103 based on the combination of Au-Young and Green is improper and should be withdrawn.

Au-Young in view of Thorpe

In paragraph 12 of the Office Action, the Patent Office maintains the rejection of claims 1-3, 77, 80-82, and 85-86 under 35 U.S.C. §103(a), as allegedly unpatentable over Au-Young in view of Thorpe.

Au-Young is not suggestive of the antibodies of the invention for the reasons discussed above.

For the combination of Au Young and Thorpe to render the claimed invention obvious, Thorpe must cure the deficiencies of Au-Young. Thorpe does not teach or suggest a PSCA protein or portions thereof let alone the function(s) or expression of PSCA, or portions thereof. Instead, Thorpe merely provides a general review of antibodies conjugated to cytotoxic agents (e.g., immunoconjugates). Therefore, the combination of Thorpe and Au-Young does not suggest the claimed invention and the rejection under 35 U.S.C. §103 is improper and should be withdrawn.

THE CLAIMED INVENTION POSSESSES UNEXPECTED ADVANTAGES THAT THE CITED REFERENCES DOES NOT TEACH

Applicants respectfully contend that the cited references do not render the claimed invention *prima facie* obvious. Furthermore, the alleged obviousness is rebutted by evidence of unexpected properties of the claimed invention (In re Davies and Hopkins, 177 U.S.P.Q. 381).

Applicants have provided data showing that the antibodies of the invention possess superior properties than those disclosed by the references cited herein. Specifically, applicants have provided the following.

1. The antibodies of the invention inhibit prostate tumor growth *in vivo* (page 49, lines 8-10)
2. A cocktail of 7 anti-PSCA antibodies inhibits growth of human prostate tumor xenografts in mice (Examples 18 A and B at pages 107, lines 11-30, through page 112, lines 1-15; Figures 48 and 53).
3. A single anti-PSCA antibody, designated 1G8, inhibits growth of human prostate tumor xenografts in mice (Example 18C1 at page 112 lines 17-28 through page 113, lines 1-14; Figure 54).
4. Two other anti-PSCA antibodies designated 2A2 and 2H9, administered singly, inhibit growth of human prostate tumor xenografts in mice (Example 18C2 at page 113, line 16-30; page 114, lines 1-9; Figures 55A and B).

5. Another anti-PSCA antibody, designated 3C5, inhibits growth of established prostate tumors in mice (Example 18C4 at page 114, lines 21-30; page 115, lines 1-3; Figure57).
6. Some of the antibodies of the invention are internalizing and thus are more potent anti-tumor agents (specification at page 26, lines 20-22).
7. The fragments of the antibodies of the invention are usable just like whole antibody (specification at page 21, lines 11-17; page 22, lines 23-30).
8. The antibodies of the invention induce apoptosis (specification at page 50, lines 20-22).

In view of the aforementioned discussion, applicants respectfully request that the Patent Office reconsider and withdraw the rejection of claims 2-3 under 35 U.S.C. §103.

B. NEW GROUNDS OF REJECTION

35 USC §112, SECOND PARAGRAPH

In paragraph 13, the Examiner rejected claims 1-3 and 69-86 under 35 USC §112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention.

In paragraph 13a, the Examiner indicated that claims 1-3 and 69-86 are indefinite for reciting "or a portion thereof" in claims 1-3 because the exact meaning of the phrase is not clear. The Examiner is questioning whether it means the antibody binds an amino acid of SEQ ID NO:2, an epitope contained in amino acids 2-50, 46-109, or 85-123.

Applicants respectfully disagree. However, the rejection is moot since applicants have amended the claims to delete the term "or portion thereof".

In paragraph 13b, the Examiner indicated that claim 69 is indefinite for reciting "chimeric" because the exact meaning of the word is not known.

Applicants respectfully disagree, "chimeric" is described in the originally-filed specification to mean the following: chimeric antibodies are immunoglobulin molecules comprising a human and a non-human portion. For example, the antigen-combining region (variable region) can be from a non-human source and the constant region can be from a human source (page 25, lines 1-6). Thus, withdrawal of this rejection is requested.

In paragraph 13c, the Examiner indicated that claims 79 and 84 are indefinite for reciting "131In" because the exact meaning of the term is not clear.

In response, Applicants have amended claims 79 and 84 to delete the term "^{131}In".

NEW REJECTIONS UNDER 35 USC §103

In paragraph 14, the Examiner rejected claims 1-3, 69-70, and 73-76 under 35 USC §103(a) as allegedly unpatentable over Au-Young (the '136 patent).

Au-Young does not render obvious the claimed invention for the reasons discussed above.

Au-Young in view of Hellstrom

In paragraph 15 of the Office Action, the Patent Office rejected claims 76-79 and 82-84 under 35 U.S.C. §103(a), as allegedly unpatentable over Au-Young in view of Hellstrom.

Au-Young is not suggestive of the antibodies of the invention for the reasons discussed above.

For the combination of Au Young and Thorpe to render the claimed invention obvious, Hellstrom must cure the deficiencies of Au-Young. Hellstrom does not teach or suggest a PSCA

protein or portions thereof let alone the function(s) or expression of PSCA, or portions thereof. Instead, Hellstrom teaches a murine monoclonal antibody against BR96 conjugated to I^{131} for tumor killing. Therefore, the combination of Thorpe and Au-Young does not suggest the claimed invention and the rejection under 35 U.S.C. §103 is improper and should be withdrawn.

CONCLUSION

Entry of this amendment and the foregoing remarks in the file of the above-captioned patent application is respectfully requested. Applicants believe that all grounds for rejection of the claims have been successfully overcome and that the claims are now in condition for allowance. Withdrawal of the Patent Office's remaining rejections is requested and prompt allowance of the claims is solicited. If any issues remain in connection with the claims, the Examiner is encouraged to contact the undersigned by telephone to discuss the same.

Only the fee for a three-month extension of time is deemed necessary in connection with the filing of this Amendment. The fee for the three-month extension of time is $460.00. A check for $460.00 is enclosed. If any additional fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Pages entitled "Version with Markings to Show Changes in the Claims" are attached hereto to show the changes made to the application according to this amendment.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES IN THE CLAIMS

Please amend claims 1-3 and 68-85 as follows:

--1. (TWICE AMENDED) A monoclonal antibody which recognizes and binds an N-terminal portion of a Prostate Stem Cell Antigen (PSCA) protein consisting of amino acids 2 through 50 [or a portion thereof] as described in SEQ ID NO:2 . --

--2. (TWICE AMENDED) A monoclonal antibody which recognizes and binds a middle portion of a Prostate Stem Cell Antigen (PSCA) protein consisting of amino acids 46 through 109 [or a portion thereof] as described in SEQ ID NO:2 . --

--3. (TWICE AMENDED) A monoclonal antibody which recognizes and binds a C-terminal portion of a Prostate Stem Cell Antigen (PSCA) protein consisting of amino acids 85 through 123 [or a portion thereof] as described in SEQ ID NO:2. --

--70. (TWICE AMENDED) The monoclonal antibody of claim [18] 69, wherein the chimeric antibody comprises a murine immunoglobulin variable region and a human immunoglobulin constant region. --

--71. (AMENDED) The monoclonal antibody of claim 1, 2 or 3 which is a humanized antibody. --

--72. (AMENDED) The monoclonal antibody of claim [20] 71, wherein the humanized antibody comprises a human immunoglobulin constant region. –

-- 77. (AMENDED) An immunotoxin comprising the recombinant protein of claim [25] 76 conjugated with a therapeutic agent. --

-- 78. (AMENDED) The immunotoxin of claim [26] 77, wherein the therapeutic agent is a radioactive isotope. --

-- 79. (AMENDED) The immunotoxin of claim [27] 78, wherein the radioisotope is selected from a group consisting of ^{212}Bi, ^{131}I, [^{131}In] ^{90}Y and ^{186}Re. --

-- 80. (AMENDED) The immunotoxin of claim [26] 77, wherein the therapeutic agent is a cytotoxic agent. --

-- 81. (AMENDED) The immunotoxin of claim [29] 80, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid. --

-- 83. (AMENDED) The immunoconjugate of claim [31] 82, wherein the therapeutic agent is a radioactive isotope. --

-- 84. (AMENDED) The immunoconjugate of claim [32] 83, wherein the radioisotope is selected from a group consisting of ^{212}Bi, ^{131}I, ^{90}Y and ^{186}Re. --

-- 85. (AMENDED) The immunoconjugate of claim [31] 83, wherein the therapeutic agent is a cytotoxic agent. --

-- 86. (AMENDED) The immunotoxin of claim [34] 85, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide,

vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid. --